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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,480	10/27/2003	Joseph Alan Walder	PA2003-9	7983

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INTEGRATED DNA TECHNOLOGIES, INC.
8930 GROSS POINT RD.
SUITE 700
SKOKIE, IL 60077

EXAMINER	
WHISENANT, ETHAN C	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/694,480	WALDER ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant, Ph.D.	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 JUN 06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,16-23,33 and 36* is/are rejected.

7)☒ Claim(s) *11-15,24-32,34,35 and 37-39* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

NON-FINAL ACTION

1. The applicant's response (filed 17 FEB 06) to the Office Action has been entered. Following the entry of the claim amendment(s), **Claim(s) 1-39** is/are pending. Rejections and/or objections not reiterated from the previous office action are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
>
> **(e)** the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> or
>
> **(e)** the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

3. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 102/103

6. **Claim(s) 1-10 and 18-23** is/are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Callaghan et al. [WO99/05314 (04 FEB 1999)]

Claim 1 is drawn to nucleic acid comprising : (a) a cleavage domain comprising a single-stranded region, said single-stranded region comprising at least one intenucleotide linkage 3' to an adenosine residue, at least one intemucleotide linkage 3' to a cytosine residue, at least one intemucleotide linkage 3' to a guanosine residue, and at least one intenucleotide linkage 3' to a ulidine residue, and wherein said cleavage domain does not comprise a deoxyribonuclease-cleavable internucleotide linkage, (b) a

fluorescence reporter group on one side of the internucleotide linkages; and (c) a non-fluorescent fluorescence-quenching group on the other side of the intenucleotide linkages.

Callaghan et al. teach a nucleic acid (e.g. 0007M) comprising all of the structural limitations recited in Claim 1. See, for example, lines 24-25 on p. 5. As regards the limitation " a cleavage domain" it is asserted by the examiner that this limitation is inherent to the loop portion (i.e. the cleavage domain) of the RNA molecular beacons taught by Callaghan et al. in that the loop portion of the RNA molecular beacons taught by Callaghan et al. are susceptible to chemical cleavage means.

Claim 2 is drawn to embodiment of the nucleic acid of Claim 1 wherein wherein the fluorescence-quenching group is selected from a defined group which includes is a substituted 4-(phenyldiazenyl) phenyl amine compound.

Callaghan et al. teach this limitation wherein these authors teach that the acceptor species (i.e. the quencher) may include TAMRA, Pyrene butyrate, or DABCYL i.e. 4-(4'-dimethylaminophenylazo)benzoic acid). See the last two paragraphs on p. 2.

Claim 3 is drawn to embodiment of the nucleic acid of Claim 1 wherein wherein the tluorescence-quenching group is selected from a defined group which includes 4-(4'-dimethylaminophenylazo)benzoic acid).

Callaghan et al. teach this limitation wherein these authors teach that the acceptor species (i.e. the quencher) may include TAMRA, Pyrene butyrate, or DABCYL i.e. 4-(4'-dimethylaminophenylazo)benzoic acid). See the last two paragraphs on p. 2.

Claim 4 is drawn to embodiment of the nucleic acid of Claim 1 wherein the fluorescence reporter group is selected from a defined group which includes fluorescein, tetrachlorotluorescein, hexachlorotluorescein, rhodamine, tetramethylrhodamine, a Cy dye, Texas Red, a Bodipy dye, or an Alexa dye.

Callaghan et al. teach this limitation wherein these authors teach "Examples of convenient donor species will be apparent to the scientist of ordinary skill and include FAM, TET, JOE, HEX, ROX, BODIPY and EDANS. Convenient acceptor species include TAMRA. Pyrene butyrate, and DABCYL." See the last two paragraphs on p. 2.

Claim 5 is drawn to embodiment of the nucleic acid of Claim 1 wherein wherein the fluorescence reporter group is attached to the 5'-terminal nucleotide of the nucleic acid.

Callaghan et al. teach this limitation wherein these authors teach "the donor and acceptor species are attached to the Molecular Beacons probe in any convenient way. By way of non-limiting example either species may be attached to the 3' terminus of the probe via controlled pore glass (CPG) based synthesis or attached to the 5' terminus via 5'-phosphoramidite chemistry. The donor and quencher species are attached at any convenient locations on the probes, such as for example at or near the ends of the probe, preferably at the ends of the probe." See the last two paragraphs on p. 2.

Claim 6 is drawn to embodiment of the nucleic acid of Claim 1 wherein wherein the fluorescence quenching group is attached to the 5'-terminal nucleotide of the nucleic acid.

Callaghan et al. teach this limitation wherein these authors teach "the donor and acceptor species are attached to the Molecular Beacons probe in any convenient way. By way of non-limiting example either species may be attached to the 3' terminus of the probe via controlled pore glass (CPG) based synthesis or attached to the 5' terminus via 5'-phosphoramidite chemistry. The donor and quencher species are attached at any convenient locations on the probes, such as for example at or near the ends of the probe, preferably at the ends of the probe." See the last two paragraphs on p. 2.

Claim 7 is drawn to embodiment of the nucleic acid of Claim 1 which is a single-stranded RNA molecule.

Callaghan et al. teach this limitation wherein these authors teach : "The beacons probe is a unitary probe comprising a single stranded target complementary sequence, a stem duplex consisting of nucleotide sequences 5' and 3' to the target complement sequence and having a melting temperature lower than the target complementary sequence/target sequence melting temperature, and at least one label pair, each pair comprising a first label conjugated to the probe at or near the 5' terminus of the probe and a second label conjugated to the probe at or near the terminus of the probe. Under assay conditions, hybridisation of the target complementary sequence to the
target sequence leads to a change in Beacons signal from the label pair. See the last two paragraphs on p. 2.

Claim 8 is drawn to embodiment of the nucleic acid of Claim 1 which is a chimeric oligonucleotide comprising a nuclease resistant modified ribonucleotide residue. **Claim 9** is drawn to embodiment of the nucleic acid of Claim 8 wherein the modified ribonucleotide residue is selected from a defined group which includes 2'-O-methyl ribonucleotide.

Callaghan et al. teach these limitations see, at least, for example, the absrtract.

Claim 10 is drawn to embodiment of the nucleic acid of Claim 8 wherein the modified ribonucleotide residue is at the 5-terminus or the 3' terminus.

Callaghan et al. teach this limitation in that these authors makes clear that all of the ribonucleotide residues making up their molecular beacons comprise 2'-O-substituted ribonucleotide residues.

Claim 18 is drawn to an embodiment of the nucleic acid of Claim 1 wherein wherein the fluorescence quenching group is 5' to the cleavage domain and the fluorescence reporter group is 3' to the cleavage domain.**Claim 19** is drawn to

anembodiment of the nucleic acid of Claim 18 wherein the fluorescence-quenching group is at the 5' terminus of the nucleic acid. **Claim 20** is drawn to an embodiment of the nucleic acid of Claim 18 wherein the fluorescence reporter group is at the 3' terminus of the nucleic acid. **Claim 21** is drawn to embodiment of the nucleic acid of Claim 1 wherein wherein the fluorescence reporter group is 5' to the cleavage domain and the fluorescence quenching group is 3' to the cleavage domain. **Claim 22** is drawn to an embodiment of the nucleic acid of Claim 21 wherein the fluorescence reporter group is at the 5' terminus of the nucleic acid. **Claim 23** is drawn to embodiment of the nucleic acid of Claim 21 wherein the fluorescence quenching group is at the 3' terminus of the nucleic acid.

Callaghan et al. teach these limitations wherein these authors teach "the donor and acceptor species are attached to the Molecular Beacons probe in any convenient way. By way of non-limiting example either species may be attached to the 3' terminus of the probe via controlled pore glass (CPG) based synthesis or attached to the 5' terminus via 5'-phosphoramidite chemistry. The donor and quencher species are attached at any convenient locations on the probes, such as for example at or near the ends of the probe, preferably at the ends of the probe." See the last two paragraphs on p. 2.

RESPONSE TO APPLICANT'S AMENDMENT/ ARGUMENTS

7. Applicant's arguments with respect to the claimed invention have been fully and carefully considered but are not deemed to be persuasive.

The applicant traverses the rejection of Claim 1 over Theaker et al. (i.e. Callaghan et al.) arguing that the molecular beacons taght by Theaker et al. (i.e. Callaghan et al.) do not comprise a cleavage domain. The examiner disagrees. The loop region is cleavable by, for example, chemical means. The fact that Theaker et al. (i.e. Callaghan et al.) do not teach cleaving this domain (i.e. the loop region) does not

mean that said domain is not cleavable. Any of the internucleotide linkages within the 2'-O-substituted RNA molecular beacons taught by Theaker et al. (i.e. Callaghan et al.) are cleavable by, for example, chemical means. See for example p. 436 of Diamond et al. [Methods in Enzymology 100 : 431-453 (1983)]. Therefore, it is asserted that the molecular beacons taght by Theaker et al. do comprise a cleavage domain.

A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re Casey* , 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963). It is noted that "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

The applicant also argues that Theaker et al. (i.e. Callaghan et al.) teaches away from applicant's invention. The question whether a reference "teaches away" from the invention is inapplicable to an anticipation analysis. Celeritas Technologies Ltd. v. Rockwell International Corp., 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir.1998) (The prior art was held to anticipate the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed."). See also Atlas Powder Co. v. IRECO, Inc., 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999)(Claimed composition was anticipated by prior art reference that inherently met claimlimitation of "sufficient aeration" even though reference taught away from air entrapment or purposeful aeration.). The examiner made a 102/ 103 rejection only to demonstrate to the applicant that the examier was relying upon the theory of inherency to make the anticipation rejection.

Please note that the Callaghan et al. [WO99/05314 (04 FEB 1999)] reference is identical to the Theaker et al. [US 2002/0102571 (2002)] reference cited in the previous Office action, however it has a 102(b) date of 04 FEB 1999 rather than a 102(e) date. As such it is the best prior art discovered during the search and should have been cited in said previous Office action. That oversight has been corrected herein in order to crystalize the issue(s) should the applicant choose to appeal the examiner's decision.

CLAIM REJECTIONS UNDER 35 USC § 103

8. **Claim(s) 16-17 is/are** rejected under 35 U.S.C. 103(a) as being unpatentable over Callaghan et al. [WO99/05314 (04 FEB 1999)] as applied against Claim 1 above and further in view of Tyagi et al. [US 6,037,130 (2000)].

Claim 16 is drawn to embodiment of the nucleic acid of Claim 1 which is 5-30 nucleotides in length. **Claim 17** is drawn to embodiment of the nucleic acid of Claim 16 which is 5-30 nucleotides in length.

Callaghan et al. teach a nucleic acid comprising all of the limirtatons recited in Claim 16 except these authors do not teach that the nucleic acid of their invention be 5-30 nucleotides in length. However, Tyagi et al. do teach the structural length constraints of molecular beacon probes : "Molecular beacon probes may have target recognition sequences 7-140 nucleotides in length and arms that form a stem hybrid, or "stem duplex" 3-25 nucleotides in length. Modified nucleotides and modified nucleotide linkages may be used." Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Callaghan et al. wherein their molecular beacon probes are 5-30 nucleotides in length and/or 7-10 nucleotides in length. The ordinary artisan would have been motivated to make this modification in order to reducr the cost of oligonucleotide synythesis.

9. Claim(s) 33 and 36 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Callaghan et al. [WO99/05314 (04 FEB 1999)] as applied against Claim 1 above and further in view of Coull et al. [US 6,355,421(2002)]` (2000)].

Claim 33 is drawn to a kit comprising a substrate said substrate comprising a nucleic acid as recited in Claim 1.

As argued above Callaghan et al. teach a nucleic acid comprising all of the limitatons recited in Claim 1. In addition, Callaghan et al. teach kits comprising the nucleic acid probes of their invention. Callaghan et al. do not teach that the kit should comprise a substrate with the nucleic acid probe of their invention immobilized thereon. However, Coull et al. do teach molecular beacon type probes immobilized on a solid support (i.e. substrate) which they call "Molecular beacon arrays." In addition these authors teach that "molecular beacon arrays are convenient because they provide a means to rapidly interrogate numerous samples for the presence of one or more target sequences of interest in real time without using a secondary detection system. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Callaghan et al. wherein their kits comprising their molecular beacon probe(s) are immobilized on a substrate. The ordinary artisan would been motivated to make this modification in order to rapidly interrogate numerous samples for the presence of one or more target sequences of interest in real time without using a secondary detection system.

Claim 36 is drawn to the kit of Claim 33 further comprising a buffer.

Callaghan et al. teach this limitation. See, at least, for example, lines 16-18 on p. 4.

CLAIM OBJECTIONS

10. **Claim(s) 11-15, 24-32, 34-35 and 37-39** is/are objected to because it/they is/are dependent upon a rejected independent base claim.

CONCLUSION

11. **Claim(s) 1-39** is/are rejected and/or objected to for the reason(s) set forth above.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30AM - 5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

The Central Fax number for the USPTO is (571) 273-8300. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

ETHAN WHISENANT
PRIMARY EXAMINER
Art Unit 1634